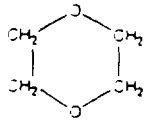
1,4-DIOXANE
CAS No. 123-91-1

First Listed in the *Second Annual Report on Carcinogens*



SDMS DocID 2050631

CARCINOGENICITY

1,4-Dioxane is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.11, 1976; NCI 80, 1978, IARC S.4, 1982). When administered in drinking water, 1,4-dioxane increased the incidences of squamous cell carcinomas of the nasal turbinates in rats of both sexes and hepatocellular adenomas in female rats. When administered in the drinking water in another study, 1,4-dioxane induced hepatocellular carcinomas in rats of both sexes. When administered in the drinking water, the compound induced hepatomas and carcinomas of the gallbladder in male guinea pigs. When administered in drinking water, 1,4-dioxane increased the incidence of hepatocellular carcinomas in mice of both sexes. As a promoter in a two-stage skin carcinogenesis study, the compound caused increased incidences of skin tumors (papillomas and squamous cell carcinomas and sarcomas) in mice of both sexes. When administered by intraperitoneal injection, 1,4-dioxane increased the incidence of lung tumors in male mice.

There is inadequate evidence for the carcinogenicity of 1,4-dioxane in humans. In a mortality study of 165 workers potentially exposed to 1,4-dioxane since 1954, two workers died from cancer (IARC S.7, 1987).

PROPERTIES

1,4-Dioxane is a volatile, colorless liquid with a mild, ethereal odor. It is miscible with water, alcohol, ether, most organic solvents, aromatic hydrocarbons, and oils. 1,4-Dioxane is flammable and may form explosive peroxides during storage. It is available in reagent, technical (more than 99.9% pure), spectrophotometric, and scintillation grades.

USE

1,4-Dioxane is used primarily as a stabilizer in chlorinated solvents, particularly 1,1,1-trichloroethane (approximately 90% of the 1,4-dioxane produced). It is also used as a solvent for cellulose acetate, ethyl cellulose, benzyl cellulose, lacquers, plastics, varnishes, paints, dyes, resins, oils, fats, waxes, greases, and polyvinyl polymers. 1,4-Dioxane is used as a reaction medium solvent in organic chemical manufacture, as a wetting agent and dispersing agent in textile processing, as a solvent for specific applications in biological procedures, as a liquid scintillation counting medium, as a reagent for laboratory research and testing, in the preparation of histological sections for microscopic examination, in paint and varnish strippers, and in stain and printing compositions (NCI DCE, 1985e). 1,4-Dioxane was also used as a solvent in coatings, sealants, adhesives, cosmetics, and pharmaceuticals, but these uses have been discontinued due to the potential carcinogenicity of the compound.

AR100025

PRODUCTION

The 1998 *Chemical Buyers Directory* identifies seven domestic suppliers of 1,4-dioxane, and *Chemcyclopedia 98* names five (Tilton, 1997; Rodnan, 1997). The current *Directory of Chemical Producers* lists two producers of the compound with undisclosed amounts (SRIa, 1997). The USITC has identified one U.S. producer of 1,4-dioxane since 1987, also without production volumes (USITC, 1988-1995). In 1986, the USITC identified two domestic producers of 1,4-dioxane. No import data were available. In 1985, four companies produced approximately 25 million lb of 1,4-dioxane, and none was imported into the United States (ICF, 1986; SRIa, 1986). There were three producers in 1984 and 1983, but U.S. production for these years was not reported (USITC, 1984, 1985). In 1982, nearly 15 million lb of 1,4-dioxane were produced by three companies in the United States (USITC, 1983). There were three producers in 1981, but no production figure was reported. Sales of 1,4-dioxane in the United States were reported to be 7.4 million lb in 1981 (USITC, 1982). The 1979 TSCA Inventory identified seven U.S. companies producing approximately 11.6 million lb, and three companies importing 1.1 million lb of 1,4-dioxane in 1977 (TSCA, 1979). Commercial production of 1,4-dioxane in the United States was first reported in 1951, but commercial quantities were produced before that time (NCI DCE, 1985e).

EXPOSURE

The primary routes of potential human exposure to 1,4-dioxane are inhalation, ingestion, and dermal contact. 1,4-Dioxane may be formed as a by-product of reactions based on condensing ethylene oxide or ethylene glycol during the production of certain consumer products. Exposure of the general population to 1,4-dioxane could possibly occur from contact with products containing residues of the compound. According to CPSC, consumers may possibly be exposed to residual levels of 1,4-dioxane formed during the manufacture of detergents, shampoos, surfactants, and certain pharmaceuticals. CPSC reported that the presence of 1,4-dioxane, even as a trace contaminant, is cause for concern. The Commission continues to monitor its use in consumer products. Residues may be present in food packaged in 1,4-dioxane-containing materials, or on food crops treated with 1,4-dioxane-containing pesticides. Potential occupational exposure to 1,4-dioxane could occur during its production and use as a stabilizer or solvent. Potential exposure of workers involved with transporting 1,4-dioxane (rail and truck) may occur due to leakage from bulk loading lines. The National Occupational Exposure Survey (1981-1983) indicated that 86,489 workers, including 30,542 women, potentially were exposed to 1,4-dioxane (NIOSH, 1984). This estimate was derived from observations of the actual use of the compound (25% of total observations) and the use of tradename products known to contain the compound (75%). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 334,000 workers were potentially exposed to 1,4-dioxane, including 100,000 workers possibly exposed as a result of 1,4-dioxane contamination of 1,1,1-trichloroethane (NIOSH, 1976). In 1977, NIOSH estimated that 2,500 workers were potentially exposed to 1,4-dioxane in the workplace, in addition to the 100,000 workers possibly exposed to both 1,1,1-trichloroethane and 1,4-dioxane (NIOSHb, 1979c). OSHA reported that as many as 466,000 workers may possibly be exposed to 1,4-dioxane in the workplace. Jobs involving transfer and handling of 1,4-dioxane in a production plant involve the greatest potential for exposure, with concentrations of up to 32 ppm. Samples taken near points of 1,4-dioxane emission in production plants indicated concentrations of up to 108 ppm, and in the vicinity of storage tanks the concentration of 1,4-dioxane was as high as 800 ppm (NCI DCE, 1985e). The ACGIH recommended threshold limit value (TLV) is 25 ppm (90 mg/m^3) as an 8-hr time-weighted average (TWA) with no short-term exposure limit (STEL) (ACGIH, 1986).

AR100024

1,4-Dioxane has a high potential for entering the environment due to its volatility and solubility in water. Emissions to the atmosphere can occur at the sites of manufacture and use of 1,4-dioxane. The Toxic Chemical Release Inventory (EPA) estimated that 352,363 lb of 1,4-dioxane were released to the environment from 43 facilities that produced, processed, or used the chemical in the United States in 1996. Of that total, 64.4% was released to water, 34.0% to air, and 1.6% to land. Ten facilities producing > 10,000 lb of 1,4-dioxane accounted for 52.5% of the total air emissions, and one facility located in Kingsport, Tennessee, reporting for the industrial classifications for manufacture of cellulosic man-made fibers (SIC Code 2823), plastics materials and resins (2821), industrial organic chemicals not elsewhere listed (2869), cyclic crudes and intermediates (2865), and printing ink (2893), represented 42.0% of total water releases (TRI96, 1998). Spent solvents disposed of improperly can contaminate ground and surface waters, and 1,4-dioxane has been detected in surface waters in the United States (CHIP, 1979a).

REGULATIONS

EPA regulates 1,4-dioxane under the Clean Air Act (CAA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Food, Drug, and Cosmetic Act (FD&CA), Resource Conservation and Recovery Act (RCRA), and Superfund Amendments and Reauthorization Act (SARA). CAA establishes control technology standards for emissions of 1,4-dioxane, and a reportable quantity (RQ) of 100 lb has been established under CERCLA. 1,4-Dioxane is exempted from tolerances for pesticide chemicals in or on raw agricultural commodities, and it has been classified as a toxic inert ingredient of pesticide products. RCRA subjects 1,4-dioxane wastes to report/recordkeeping requirements, and SARA lists it as a toxic chemical and sets general threshold amounts for producing and using 1,4-dioxane at a facility. FDA regulates 1,4-dioxane under FD&CA as an indirect food additive when it is used as an adhesive component in packaging materials. FDA is surveying raw materials and products contaminated with 1,4-dioxane. NIOSH recommended an exposure ceiling of 3.6 mg/m^3 (1 ppm) sampled over a 30-minute period. NIOSH based this recommendation on the carcinogenic effects of 1,4-dioxane in animal studies. OSHA adjusted the permissible exposure limit (PEL) to 90 mg/m^3 (25 ppm) as an 8-hr time-weighted average (TWA) for 1,4-dioxane in the workplace. This standard was based on toxic effects other than carcinogenicity. OSHA regulates 1,4-dioxane under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-56.